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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,794	03/23/2001	Robert S. Lowe	20276P	1127

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EXAMINER

GUZO, DAVID

ART UNIT PAPER NUMBER

1636

DATE MAILED: 02/28/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,794

Applicant(s)

LOWE ET AL.

Examiner

David Guzo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-10 and 12 is/are allowed.
- 6) ☒ Claim(s) 11 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

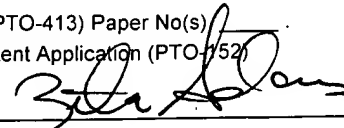
Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-752)
- 6) ☐ Other: 

DETAILED ACTION

If applicant desires priority under 35 U.S.C. 120 or 119(e) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the

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claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but instead is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

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1. Unpredictability of the art. The art with regard to vaccines against HPV infections in humans or with regard to use of chimeric HPV VLPs as vaccines against other pathogens must be considered to be extremely unpredictable. As noted by Konya et al. (Adv. Cancer Res., 2001, Vol. 82, Abstract), "The cellular immunity to HPV is implicated as an important factor in cervical carcinogenesis, but the main targets and types of responses that mediate HPV clearance are not established." The use of animal models for human diseases can provide important clues in developing vaccines for humans; however, as noted by Nicholls et al. (Veterinary Immunology and Immunopathology, 2000, Vol. 73, pp. 101-127) the ability of animal models to duplicate the natural infection process (and pathogenesis) of HPVs in humans is generally poor or unknown. Nicholls et al. also underscores the complex interplay of host and viral factors governing the outcome of infection by different HPVs in humans (and other animal species) and the added complexity this introduces in the development of efficacious vaccines against HPV infections. With regard to use of chimeric HPVs comprising a capsid protein fused with another HPV protein (such as E3, E6, E7, etc.) as potential vaccines, Greenstone et al. (PNAS, 1998, Vol. 95, pp. 1800-1805) notes that while said chimeric HPVs may induce generation of class I-restricted CTLs in mice, the potential for HPV VLPs to function as a therapeutic vaccine in humans is unknown and must await years of further research and trials.

With regard to use of chimeric VLPs as recombinant vaccines against pathogens other than HPV, it is unpredictable whether the HPV VLPs will present the foreign protein to the host immune system in a manner sufficient to raise a protective humoral

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and/or cell mediated immune response. For example, if the VLPs comprise a HIV protein (such as Tat) and are to be used as a vaccine against HIV infection, it is unclear if the VLPs can present the HIV protein to the immune system in a manner sufficient to provide protection against HIV infection. Likewise, if the vaccine is directed against a pathogen such as HCV or poliovirus which is restricted to specific tissues in the body, it is unclear if the VLPs carrying the protein derived from the pathogen can elicit the proper immune response against the pathogen in the tissues affected by said pathogen. With regard to attempts to generate vaccines against pathogens such as HIV, HCV, malaria, etc., Cohen (Science, 1994, Vol. 265, pp. 1371-1373) recites Jonas Salk as saying that scientists researching vaccine development "don't have a clue" as to what is required to make an effective vaccine and that "There's going to be a need for more awareness not of the pathogen, but of the host".

2. State of the art. The art in this area is undeveloped. At the time of applicants' invention, no recombinant vaccine against HPV infection in humans had been unambiguously demonstrated. The relative roles of humoral vs. cellular immune responses in mediating HPV wart regression in humans are still poorly known. The role of cytokines in lesion regression is likewise poorly understood and the factors underlying the presence or absence of HPV-specific tumor-specific T-helper (Th) immunity in the immune response against HPV E7 expressing tumors are not known. The use of recombinant HPV VLPs as vaccines against unrelated pathogens in humans had not been attempted and is merely a theoretical possibility.

3. Scope of the invention. The claimed invention is broad and reads on a HPV based VLP vaccine comprising a polypeptide from any pathogen. Hence the claim reads on a vaccine against HPV or any pathogen from which the second polypeptide is derived (i.e. the pathogen could be HIV, HCV, etc.).

4. Number of working examples. Applicants present no working examples of the claimed invention.

5. Amount of guidance presented by applicants. Applicants present no guidance concerning the dosage of the VLPs required to vaccinate an individual against any given disease, the schedule of inoculations required, the modes of delivery of the vaccine, etc.

6. Nature of the invention. The invention involves one of the most complex areas of molecular biology/medicine, the generation and use of recombinant VLPs as vaccines against HPV infection and infection by any other pathogen in humans.

7. Level of skill in the art. The level of skill in the art is high; however, given the unpredictability of the art, the poorly developed state of the art, the lack of guidance presented by applicants and the broad scope of the claims, it must be considered that the skilled artisan would have needed to conduct trial and error experimentation in order to attempt to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites a vaccine comprising a HPV VLP comprising HPV proteins a second protein from another source. It is therefore unclear what pathogen the vaccine is directed against, i.e. HPV or the pathogen from which the second protein was derived.

The closest prior art relating to the claimed invention is Lowy et al. (U.S. Patent 5,855,891). Lowy et al. teaches generation of recombinant HPV VLPs comprising fusions between the full length HPV L2 protein and other proteins. Lowy et al. does not teach or suggest use of shortened L2 proteins in the fusion constructs.

1-10 and 12 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
February 25, 2002

DAVID GUZO
PRIMARY EXAMINER
